REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and the following commentary.

I. Status of the Claims

Claims 1-26, 52-53 and 108-109 were cancelled previously. Claims 51 and 107 are cancelled in this response without prejudice or disclaimer thereof. Claims 27 and 87 have been amended to exclude a non-steroidal anti-inflammatory drug (NSAID) as an active agent. Exemplary support for the amendments can be found in the original specification, for example, at page 6, line 15; and at page 17, line 23.

Applicants acknowledge the finality of the outstanding Office Action. Nevertheless, because no additional search is required for the amendments to the claims, and because the amendments do not introduce new matter and either place the application in condition for allowance or at least in better condition for appeal, Applicants respectfully request entry of this amendment. Upon entry, claims 27-50 and 87-106 will be under examination, with claims 54-86 and 110-111 withdrawn.

II. Rejection of Claims under 35 U.S.C. § 112, first paragraph

Claims 27-51 and 87-107 are rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of written description. Claims 51 and 107 are cancelled thereby mooting the rejection. Applicants respectfully traverse the rejection of the remaining claims.

Specifically, the Examiner contends that the negative limitations excluding ketoprofen and naproxen as active agents are not supported by the specification. Pursuant to MPEP 2173.05(i), an element may be explicitly excluded in the claims if the element is positively recited in the specification. *In re Johnson*, 558 F.2d 1008, 1019, 194 USPQ 187, 196 (CCPA 1977). In the present case, the specification identifies ketoprofen and naproxen as the active

agents of the claimed composition (Examples 3-12), which provides sufficient support for excluding these compounds from the claimed composition.

By the same token, the present claims excluding a non-steroidal anti-inflammatory drug (NSAID) are supported by the specification, because NSAID is explicitly disclosed in Example 1.

Accordingly, Applicants respectfully request withdrawal of the rejection.

III. Summary of the Claimed Invention

The claimed invention is directed to the surprising and unexpected discovery of a new rapidly disintegrating solid dosage form. The claimed compositions comprise: (1) a poorly soluble nanoparticulate active agent that is not an NSAID, having an effective average particle size of less than about 2 microns; (2) a surface stabilizer adsorbed on the surface of the active agent; and (3) at least one pharmaceutically acceptable water-soluble or water-dispersible excipient.

The rapidly disintegrating solid oral dosage form of the invention has the advantage of combining: (1) rapid presentation of the poorly soluble active agent that is not an NSAID as a result of the rapid disintegration, and (2) rapid dissolution of the poorly soluble drug in the oral cavity as a result of the nanoparticulate size of the drug. This combination of rapid disintegration and rapid dissolution is significant, as it reduces the delay in the onset of therapeutic action associated with prior known rapidly dissolving dosage forms of poorly soluble drugs.

The claimed compositions are not taught or suggested in the prior art, as discussed in more detail below.

IV. Rejection of Claims under 35 U.S.C. §102

A. Eickhoff

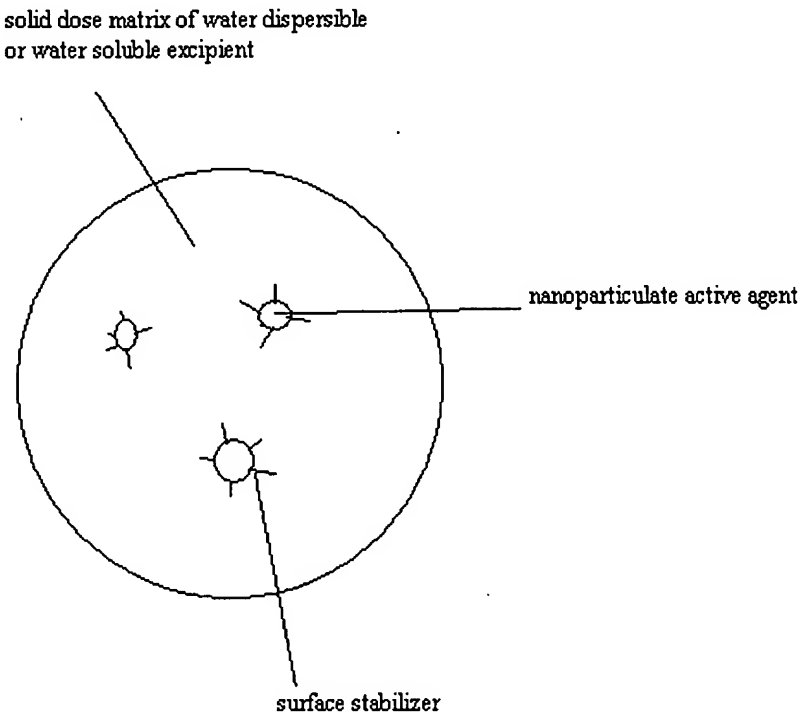
Claims 27-34, 37-47, 50-51, 87-93 and 96-107 are rejected under 35 U.S.C. §102(b) for alleged anticipation by U.S. Patent No. 5,518,738 to Eickhoff et al. ("Eickhoff"). Claims 51 and 107 are cancelled. Applicants respectfully traverse the rejection of the remaining claims.

The Examiner indicates that Eickhoff discloses a composition comprising a crystalline NSAID, such as ketoprofen and naproxen, having polyvinylpyrrolidone adsorbed on the surface thereof, hygroscopic sugar and sodium lauryl sulfate. The composition of Eickhoff exhibits reduced gastric irritation and/or hastened onset of action (abstract).

The claimed invention differs from the prior art reference in a number of aspects, namely the presently claimed invention relates to a solid dose matrix oral dosage form. The solid dose matrix comprises at least one pharmaceutically acceptable water-soluble or water-dispersible excipient, and a nanoparticulate active agent composition comprising a poorly soluble active agent that is ***not*** an NSAID and at least one surface stabilizer, as recited in claims 27 and 87. Further, the claimed formulation rapidly disintegrates upon contact with saliva in less than three minutes.

The Examiner acknowledges that "Eickhoff is silent about such [a] characteristic or property of the surface stabilizer or the formulation," but asserts that "such [a] property or characteristic [is] deem[ed] to be inherent to the referenced composition since the essential components of Eickhoff are identical to the instant composition" (Office Action, page 4, lines 14-20). The Examiner's analysis fails to acknowledge that the components of the claimed invention are modified by the functional limitation requiring rapid disintegration upon contact with saliva. Such dosage forms are frequently referred to as "fast melt" dosage forms. The matrix of at least one water-soluble or water-dispersible excipient within which the nanoparticulate composition is dispersed enables this rapid dissolution. A composition

comprising the same components but having a different structure, such as the composition of Eickhoff, does not have the rapid dissolution required by Applicants' claimed invention. *See e.g.*, the graphical depiction below of the claimed composition.

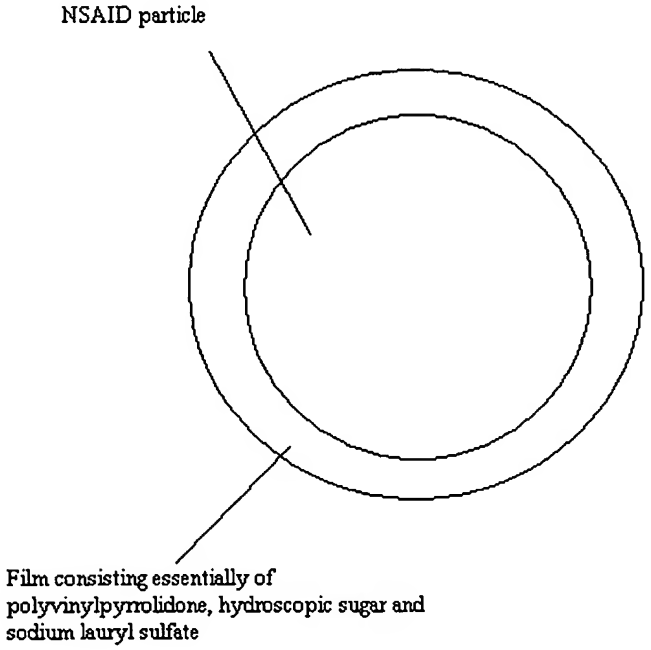


Thus, the Examiner's inherency argument effectively eliminates Applicants' required rapid dissolution claim limitation, as the Examiner is inferring that all compositions comprising the same components would have this functional feature. This conclusion is false.

Pursuant to MPEP 2112, the prerequisite for a rejection based on "inherency" is that the prior-art product must appear to be "substantially identical" to the claimed product. The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993) "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the

reference, and that it would be so recognized by persons of ordinary skill. ***Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient***.' " *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999). "In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy,* 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990).

The rapidly disintegrating element of the claimed invention does not flow from the composition of Eickhoff. Specifically, as noted above, Eickhoff requires a dosage form having a "coating" or film comprising polyvinylpyrrolidone, a hydroscopic sugar, and a sodium lauryl sulfate. A "film" structure is not the same as the claimed "matrix" structure, as graphically depicted below.



This is significant, as the film or coating structure of Eickhoff results in reduced gastric irritation following oral administration; i.e., the film inhibits the NSAID present in the composition from irritating the stomach. The is contrary to the claimed invention goal of rapid disintegration of the dosage form shortly after oral administration, as the "matrix" structure of the claimed invention does not function as a film or coating which would protect the stomach from irritation caused by the component drug.

The Examiner's allegation that the prior art meets every limitation of the claim is based on inherency. However, the Examiner has made an inherency argument for a composition that does not exist in the prior art. The Examiner first constructs the argument by creating a prophetic composition by picking and choosing a combination of elements that are *merely* stated within the text of the prior art and then attributing inherent properties to the prophetic composition. The Examiner has not provided a scintilla of evidence to support that such a determination necessarily flows from the teachings of the prior art. The probabilities and possibilities are numerous and varied and the mere fact that the claimed invention may result from a combination of there probabilities and possibilities is insufficient to establish a case of inherency. Therefore, the claimed invention is not anticipated or rendered obvious over Eickhoff.

Moreover, in sharp contrast to Eickhoff's composition of NSAID, the present claims are drawn to a rapidly disintegrating formulation comprising, *inter alia*, an active agent that is ***not an NSAID***, wherein the composition rapidly disintegrates upon contact with saliva in less than three minutes. Accordingly, Eickhoff does not anticipate the claimed invention.

B. Kerkhof

Claims 27-48, 50-51, and 87-107 are rejected under 35 U.S.C. §102(e) for alleged anticipation by PCT publication No. WO 01/45674 by Kerkhof et al. ("Kerkhof"). Claims 51 and 107 are cancelled. Applicants respectfully traverse the rejection of the remaining claims.

Similar to Eickhoff, the Examiner acknowledges that Kerkhof is silent about the rapid disintegrating or dissolving profiles of the claimed composition but relies on the rationale of "inherent properties" for the rejection (Office Action, paragraph bridging pages 6 and 7).

As discussed *supra*, the fast-melting property of the claimed composition is achieved by the combination of rapid disintegration and rapid dissolution of the solid dose matrix and the active agent, which effect is significant, as it reduces the delay in the onset of therapeutic action. One skilled in the art would have recognized that the disclosed "stability" property of Kerkhof's composition is irrelevant to the rapid disintegration and dissolving profiles of the claimed composition. Moreover, except for the laundry lists of active agents described at pages 9 and 10, surface modifiers at page 11, and carrier excipient at page 8, Kerkhof provides no guidance whatsoever on how to make and use the claimed composition that disintegrates or dissolves upon contact with saliva in less than about 3 minutes.

Applicants note that the Examiner's rationale of rejection seems incomplete (Office Action, page 12, line 4, "In this case..."). Therefore, Applicants cannot respond to the incomplete analysis at this time.

In view of the foregoing, neither Eickhoff nor Kerkhof teaches or suggests the claimed invention. Withdrawal of the rejection is respectfully requested.

V. Rejection of Claims under 35 U.S.C. §103(a)

Claim 49 is rejected under 35 U.S.C. § 103(a) for alleged obviousness over Eickhoff or Kerkhof, and further in view of applicant's admitted prior art of record ([specification], page 3, lines 13-22). Applicants respectfully traverse the rejection.

Eickhoff and Kerkhof are discussed in the foregoing paragraphs. The Examiner cited the content of the specification for its alleged teaching of freeze drying technology applied to the composition of the invention. This content does not remedy the deficiencies of Eickhoff or

Kerkhof. Claim 49 is non-obvious because it depends from a non-obvious base claim 27. Accordingly, Applicants respectfully request withdrawal of the rejection.

VI. Nonstatutory Double Patenting Rejection

Claims 27-51 and 87-107 are rejected under the judicially created doctrine of double patenting over claims 1-24 and 51-70 of U.S. Patent No. 6,316,029. Claims 27-51 and 87-107 are rejected under the judicially created doctrine of double patenting over claims 1-16 and 21 of U.S. Patent No. 6,165,506, and further in view of the applicant's admitted prior art of record ([specification], page 3, lines 13-22).

Upon indication of any allowable claims, Applicants will consider submitting terminal disclaimers to overcome the nonstatutory double patenting rejections.

CONCLUSION

The present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741.

If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date June 20, 2008

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